UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/398,253	09/17/1999	MICHAEL NEHLS	8535-026-999	9822

20583 7590 07/02/2003

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	25

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/398,253	NEHLS ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10 and 12* is/are pending in the application.

4a) Of the above claim(s) *5-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *24* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Amendment responds the Amendment received on April 7, 2003 (Paper No. 23).

Claim Objections

The objection of claim 11 for depending of a non-elected claim, made in the Office Action mailed on November 5, 2002 is withdrawn in view the Amendment received April 7, 2003, canceling the claim.

Claim Rejections - 35 USC § 112

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on November 5, 2002 is withdrawn in view of the Amendment received on April 7, 2003, amending the claim.

Claim Rejections - 35 USC § 101 & 112 first paragraph-enablement

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 1, 3, 4, and 10 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility, made in the Office Action mailed on November 5, 2002 is maintained for the reasons of record. The newly filed claim 12 also falls under this rejection.

Applicants' arguments received on April 7, 2003, have been carefully and fully considered but they are not found persuasive as explained below.

Applicants' arguments are addressed in the order they were presented.

Applicants indicate that the technology of gene trap vectors allow selective isolation of genes which are involved in late stages of stem cell differentiation (pages 3-4). Therefore, Applicants argue that the gene trap method allows one to identify genes that do not have an easily observable phenotype. Whether or not the gene trap method allows for identification of genes which are low in copy number is irrelevant to the patentability of the products (i.e., polynucleotide and oligonucleotides) absent secondary characteristics attributed to the products by the method. The products of the instant application are drawn to isolated polynucleotides and oligonucleotides defined by their SEQ ID Numbers. The method of isolation (i.e., gene trap method) does nothing to the physical structure of the products and therefore, the method of their isolation (page 6, Response) is determined to be irrelevant to the patentability of the products.

Although Applicants assert that the gene trap method allows one to identify genes that do not have an ***easily observable phenotype*** (page 4, middle paragaraph), neither the specification nor the response disclose any associated phenotypes for the claimed polynucleotides. Additionally, Applicants argue it is not necessary to disclose what roles SEQ ID Numbers 9-18 play in the later stages of cellular differentiation and development in order to satisfy the specific utility requirement because the claimed oligonucleotides or polynucleotides of the present invention is not just any piece of nucleic acid (page 4, bottom), thereby satisfying the specific utility requirement. To this end, all nucleic acids are specific to their complements. In other words, for example, a piece of nucleic acid isolated from a brain cell would be specific to its complement. However, 35 USC 101, requires that the specification disclose at least one utility that is specific ***and*** substantial, as well as credible (absent a showing of well established utility,

which would presume that the utility was credible). The claims have been rejected because the specification failed to disclose at least one utility that is substantial.

On page 4, Applicants argue that the claimed oligonucleotides and polynucleotides are specifically identified and functionally validated exons. It is vague as to what functions Applicants are referring since neither the specification nor the Applicants' response disclose what the functions of the claimed polynucleotides are.

Applicants argue that the claimed polynucleotides and oligonucleotides can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites that can be used as diagnostics.

This argument is not found persuasive for the below reasons.

Although the claimed polynucleotides and oligonucleotides ***can be used*** to design primers for use in amplification assays to detect mutations within exons, introns, splice sites that can be used as diagnostics, a skilled practitioner would not know, ***previous to further experimentation***, what immediate benefit to expect from using the claimed polynucleotides and oligonucleotides. In other words, the specification would only force the skilled practitioner to further experiment on the polynucleotides/oligonucleotides in order to arrive at a "successful conclusion" of what they are useful for because Applicants have failed to recite what conditions the polynucleotides/oligonucleotides would reveal (i.e., an immediately apparent utility). A "success conclusion," as expressed in Brenner v. Manson, requires that the claimed invention have either an immediately apparent or fully disclosed "real world" utility, to which the instant specification lacks.

Applicants continue to state that the claimed polynucleotides and oligonucleotides ***are useful*** because exon splice junctions are particularly important in the study of disease and cancer because splice junctions can often be hot spots for erroneous events leading to these disease states (page 6). Such statement, at best, is guessing at a substantial utility. However, there are no evidence or example in the specification which indicate that the claimed polynucleotides and oligonucleotides have any correlation to diseases or cancers. Such logic is tantamount to saying that any segment of nucleic acid within BRCA1 and 2 genes would be useful because mutations in BRCA1 and 2 genes are known to have correlations with breast/ovarian cancers. The court in *Kirk* (at page 53) held:

We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the ***usefulness of a claimed compound in terms of possible use so general as to be meaningless*** and then, after his research or that of his competitors has **definitely ascertained an actual use for the compound**, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.

Applicants refer to Venter *et al.* (2001, Science 291:1304) on page 6 of the Response, stating that the artisans demonstrate the significance of expressed sequence information in the structural analysis of genomic data and how validated sequences provide physical evidence that effectively trumps the hypothetical conclusions provided by bioinformatics analysis of the corresponding genomic region conducted without supporting physical data. To this end, any

expressed nucleic acid would serve for the same purpose, where such use is for further research of the subject matter itself.

Applicants list six U.S. Patents which are drawn to a microarray comprising polynucleotides or oligonucleotides. Among the cited patents, five of the patents, specifically, '934, '752, '305, '501, and '776, are drawn to generic microarrays. The substantial utility of a generic microarray (without the actual SEQ ID Numbers) would be in its ability to analyze numerous genes simultaneously, an immediately apparent utility. In other words, a skilled practitioner would understand what benefit would be gained by using a microarray. However, a microarray comprising the claimed polynucleotide or oligonucleotide sequences would directly be dependent on the substantial utility of the claimed sequences. This is precisely what is found in '832 patent. On column 2, lines 49-63, the '832 patent discloses that the polynucleotide sequences of the microarray are for detecting mutations associated with cystic fibrosis in exon 4, 7, 9, 10, 11, 20, and 21 of the CFTR gene (lines 50-51), wherein the claimed sequences have correlation with cystic fibrosis disease. Based on this information, the skilled artisan would understand what immediate benefit would be realized from using the above microarray – detection of cystic fibrosis. The instant application discloses no such information other than general statements which could be true or false, verifiable only after conducting ***further research*** on the claimed polynucleotides and oligonucleotides. Therefore, based on the instant disclosure the claimed polynucleotides and oligonucleotides, even if comprised on a microarray, would not provide an immediate benefit except for providing a starting point for the skilled artisan to further experiment in order to arrive at the point of immediate "real world" use.

Applicants refer to using the claimed polynucleotides and oligonucleotides to identify polymorphisms in coding regions and associating those polymorphism with disorders in general. A "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the *presence* or a polymorphism by analyzing multiple members of the species, i.e., analyzing a population. While one can detect the absence (or presence) of a specific allele of the polymorphism in a specific individual member of the species, one cannot detect the *absence* of a polymorphism *per se* based on one individual alone. The absence of a particular allele necessarily means that a different allele is present. The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves to open the possibility that there may be no polymorphism to detect. The specification generally teaches using the claimed polynucleotides and oligonucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed polynucleotides and oligonucleotides, but fails to teach the polymorphism.

With respect to the "real world" value of ESTs in general (page 9), it is asserted that there is an "entire industry established based on the use of gene sequences or fragments from genes in a gene chip format." Applicants are advised that the patentability of subject matter is based on the statues and not on whether the industry is or is not established. While an industry might be built on microarrays being bought and sold, the patentability of the polynucleotides and/or

oligonucleotides fixed thereon must fulfill the utility requirement under 35 U.S.C. 101, to which the instant invention fails to fulfill.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3, 4, and 10 under 35 U.S.C. 112, first paragraph because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, made in the Office Action mailed on November 5, 2002 is maintained for the reasons of record. The newly filed claim 12 also falls under this rejection.

Applicants' arguments received on April 7, 2003 have been carefully and fully considered but they are not found persuasive for the reasons set forth above.

The rejection of claims 1, 3, 4, and 10 under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, made in the Office Action mailed on November 5, 2002 is maintained for the reasons of record. The newly filed claim 12 also falls under this rejection.

Applicants' arguments received on April 7, 2003 have been carefully and fully considered but they are not found persuasive for the reasons set below.

The issue is whether Applicants were in possession of the genus being claimed. This genus is not restricted to any particular disclosed subgenus or species, such as vectors

comprising the polynucleotides/oligonucleotides of the claimed SEQ ID Numbers as inserts. The only polynucleotide/oligonucleotide described by complete structure are those that consists of SEQ ID Number 9, 10, 12, 13, 17, and 18. While it is acknowledged that Applicants need not describe "every nuance" of the claimed invention, the written description must bear a reasonable correlation to that which is claimed. The disclosed subgenus and species embraced by the claims are not representative of the entire genus being claimed. The genus of nucleic acid molecules being claimed embraces any and every type of nucleic acid molecule that comprises the claimed SEQ ID Numbers, and additional sequences of any size and sequence. Clearly, at the time of filing, Applicants were not in possession of genomic materials that contain the claimed polynucleotide fragment, which are embraced by the open-ended language of the claims. The specification does not disclose what characteristics these additional sequences may or may not have that are consistent with the operability of the nucleic acid molecules as probes or primers for detection of the claimed SEQ ID Numbers in a target sequence, and all disclosed uses for the claimed nucleic acid molecules are fundamentally as probes or primers, at least in some aspect. The specification does not disclose encoding sequences or open reading frames (ORFs).

With respect to full length mRNAs, cDNAs and genomic sequences, one skilled in the art would reasonably conclude that the claims embrace these nucleic acid molecules, and the specification provides no physical (i.e. structural) characteristics of these molecules to distinguish them from other nucleic acid molecules comprising the claimed SEQ ID Numbers and no other indication that would suggest Applicants possessed them. This particular subgenus embraced by the claims has a disclosed potential utility not possessed by those members of the

claimed genus useful only in hybridization. Full length mRNAs, cDNAs and genomic sequences (genes) would encode the corresponding protein(s).

A fundamental issue here is specific to the very narrow class of product that is polynucleotide molecules. The basic question upon which Applicants and the Examiner disagree is whether the disclosure of a partial sequence of otherwise uncharacterized nucleic acid molecules that may encode a corresponding protein is sufficient to establish possession of a broad genus based solely on the description of the partial sequence, where the broad genus embraces the uncharacterized nucleic acid molecules by default. The subgenus of uncharacterized nucleic acid molecules that encode any corresponding protein is explicitly alluded to in the specification, and disclosed as possessing an additional use *not* possessed by any other members of the broad genus being claimed, i.e. encoding the protein. The specification fails to provide any structural or functional characteristic for these desired nucleic acid molecules, which encode the protein, that would distinguish them from the other members of the genus, which simply comprise the claimed SEQ ID Numbers as the sole distinguishing feature. As stated in *University of California v. Eli Lilly and Co.* at page 1404:

> An adequate written description of a DNA ... "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

That Applicants' claims embrace nucleic acid molecules that encode a corresponding protein, whatever it may be, is clearly evident from the claim language chosen. The Court in *University of California v. Eli Lilly and Co.*, at page 1405, further noted regarding generic claims:

> A written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe* , 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . .").

In the instant case, the only species specifically enumerated are the nucleic acid molecules of SEQ ID Numbers 9-18. The specific embodiments that in addition to the claimed

SEQ ID Numbers include nucleic acids that will allow the corresponding protein to be encoded cannot be predicted without the coding sequence itself. This coding sequence has not been disclosed. Clearly, the specification would not show one skilled in the art that these desired subcombinations were possessed by the Applicants, and thus the embracing genus was also not possessed.

Therefore, the claims are rejected for lacking written description as required under 35 U.S.C. 112, first paragraph.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348.

The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

6/24/03

JEFFREY SIEW
PRIMARY EXAMINER
6/24/03